

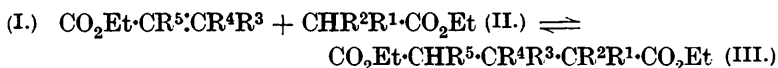
CCXLVII.—*The Correlation of Additive Reactions with Tautomeric Change. Part V. The Structural Conditions affecting Mobility and Equilibrium in Additive Reactions.*

By KENNETH ERNEST COOPER, CHRISTOPHER KELK INGOLD,  
and EDITH HILDA INGOLD.

IN various papers published during the past five years \* attention has been directed to the close analogy between mobile-hydrogen tautomerism and reversible additive reactions (8). One of the objects of this paper is to attempt to correlate the previous results and to show that the analogy extends to the structural conditions which control the mobility and equilibrium of the reversible changes.

\* The papers are denoted in the text by the following numbers : (1) C. K. Ingold and Perren, J., 1921, **119**, 1582; (2) *Idem, ibid.*, p. 1865; (3) C. K. I. and Powell, *ibid.*, p. 1976; (4) C. K. I. and Perren, J. 1922, **111**, 1414; (5) C. K. I. and Nickolls, *ibid.*, p. 1638; (6) C. K. I., Perren, and Thorpe, *ibid.*, p. 1765; (7) E. H. Ingold (Usherwood), J., 1923, **123**, 1717; (8) *Idem, Chem. and Ind.*, 1923, **42**, 1246; (9) *Idem, J.*, 1924, **125**, 435; (10) *Idem, ibid.*, p. 1319; (11) *Idem, J.*, 1925, **127**, 469; (12) Holmes and C. K. I., this vol., p. 1305; (13) C. K. I. and E. H. I., *ibid.*, p. 1310; (14) C. K. I., Shoppee and Thorpe, *ibid.*, p. 1477; (15) K. E. Cooper and E. H. I., *ibid.*, p. 1894.

The influence of structure on mobility and equilibrium may be illustrated first by reference to the Michael reaction,



the main conditions relating to which are as follows :

(a) *Groups R<sup>1</sup> and R<sup>2</sup>.* "Negative" groups, such as  $\cdot\text{CN}$  and  $\cdot\text{CO}_2\text{Et}$ , facilitate both the direct and the retrograde process, and the former group is more effective in assisting addition, and less in assisting fission, than the latter. Alkyl groups inhibit addition, and the effect is greater the larger the group.

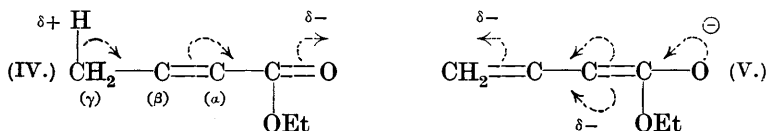
(b) *Groups R<sup>3</sup> and R<sup>4</sup>.* The presence of a  $\beta$ -substituent, and especially of two  $\beta$ -substituents, in the acrylic ester greatly reduces the tendency to addition, and the larger the groups the stronger is their inhibiting effect. This does not apply to strongly negative groups such as  $\cdot\text{CN}$  and  $\cdot\text{CO}_2\text{Et}$ , which inhibit addition very little, and may promote it.

(c) *Group R<sup>5</sup>.* An  $\alpha$ -substituent impedes addition, the effect depending on the size and polar character of the group as under (b).

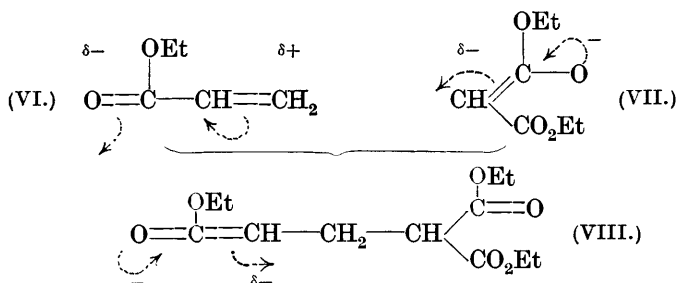
These general rules, which are based upon an experimental study of about 30 examples (1, 2, 3, 4, 5, 6, 10, 14), clearly show that combined polar and steric influences are at work (6). So far as the effect of alkyl groups is concerned, similar conditions have been shown to apply for the aldol reaction (7, 9), and it is probable that analogous rules could be formulated for the Thorpe reaction (10) and for triazan formation (15), although these reactions have not yet been studied in the same detail. Guiding principles have also been suggested (11) whereby these polar and steric effects may be partly distinguished: the chief effect of polar conditions is on mobility, addition and scission being in general simultaneously facilitated, whilst steric conditions operate mainly on the equilibrium, addition suffering greater retardation than scission.

The correlation of these additive reactions with tautomeric changes enables a further analysis of the controlling factors to be made. In a recent paper (14) the effect of structure on mobility and equilibrium in three-carbon tautomerism was interpreted on the view that the mobile hydrogen atom in three-carbon systems is in a state of incipient ionisation (compare 8, p. 1259, rule 2) owing to the pull on its binding electrons exerted by the carbethoxyl group (IV). Hydrogen in this condition can be removed from the molecule as hydron, by the action of a negative ion (12), and this enables the electron displacements, which are incipient in (IV), to proceed to completion. The ion (V) so produced tends towards a return of the

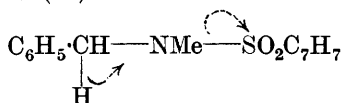
electrons to  $C_\alpha$  or  $C_\gamma$ , to which atoms, therefore, positive ions, such as hydrion, become attracted (for nomenclature, see 13):



Applying a similar mechanism to the Michael reaction in accordance with the correlation principle, we imagine that, prior to the commencement of addition, the malonic ester molecule (to take this as a definite example) has lost its hydrion and is in the condition represented by (VII) (analogous to V). Positive ions, and the positive ends of incipiently ionised molecules, will therefore be attracted to the carbon atom labelled  $\delta^-$  in (VII), and this applies to the  $\beta$ -carbon atom of acrylic ester (VI), since the pull of the carbethoxyl group on the  $\text{C}=\text{C}$  electrons will give to the  $\beta$ -carbon atom a minute positive charge ( $\delta+$ , VI) (complex ion formation; see Lapworth, J., 1901, 79, 1265, and later). As the  $\beta$ -carbon atom approaches the malonic ester molecule, so the electrons are drawn back from the ionic residue (labelled  $-$ ) and the electron displacements, originally very small, are enabled to proceed to completion. The product (VIII) is the ion of the addition compound, and the final combination with hydrion occurs at the carbon labelled  $\delta^-$  (VIII).



The corresponding retrograde process is closely analogous to the mechanism of the elimination of a sulphinate ion from a sulphonamide by hydrolysis (12):

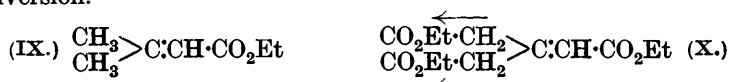


From this mechanism the combinations of polar and steric effect arising from different modifications of structure can at once be deduced.

(i) (Compare rule *a*, p. 1869.) The presence of "negative" groups (electron-sinks) in (II), since they facilitate the antecedent ionisation, will favour the addition process. They will also facilitate scission, however, as may be seen by following out the retrograde reaction, in the first step of which the tendency of the malonic ester group in (VIII) to withdraw electrons collaborates with the tendency of the ionic centre at the other end of the chain to relinquish them. This is a polar effect on mobility, and the efficacy of  $\cdot\text{CN}$  exceeds that of

$\cdot\text{CO}_2\text{Et}$ , owing to the competition  $\text{EtO}-\overset{\curvearrowright}{\underset{\curvearrowleft}{\text{C}}}=\text{O}$  which is absent in the case of  $\cdot\text{CN}$  (compare 13, 14). The steric effect of such groups has previously been discussed (3, 6) and is such as to inhibit addition. This effect is therefore one on equilibrium, and that due to  $\cdot\text{CO}_2\text{Et}$  will exceed that due to  $\cdot\text{CN}$  for spatial reasons. The polar effect of the introduction of an electron-source, such as an alkyl group (13), into (II) will be to diminish mobility, since it will tend to neutralise the charge  $\delta-$  in (VII), and also to side-track the pull upon electrons exerted by the malonic ester residue in (VIII). The steric effect, as before, will be to displace the equilibrium in the direction favouring simpler molecules (3, 6, 7, 9). All these conclusions are summarised in rule (*a*), a number of applications of which (to the aldol, as well as to the Michael reaction) are given in the papers just referred to.

(ii) (Compare rule *b*, p. 1869). The introduction of an electron-source, such as an alkyl group (13), into the  $\beta$ -position of the acrylic ester molecule must impede addition, since it will tend to neutralise the charge  $\delta+$ . Conversely, an electron-sink will, so far as its polar effect is concerned, promote addition. In either case the steric effect hinders addition, this effect being of special importance in the case of the *gem*-dialkyl group. These conclusions correspond precisely with rule (*b*), and amongst the examples which illustrate them (1, 3, 5, 6, 7, 9) are included several cases in which the steric effect to be expected from a "negative" group is either greatly diminished, or almost neutralised, or actually inverted, by the effect arising from its electron affinity. Thus (X) adds cyanoacetic ester to itself with about the same facility and degree of completeness as (IX), the electron affinity of the additional carbethoxyl groups in (X) making up for the extra space they occupy (5). The replacement of the methyl group in crotonic ester by carbethoxyl represents a case of inversion.



These considerations also adequately interpret the addition of malonic ester to citraconic ester (Hope, J., 1912, 101, 894; compare

14), one of the few known cases of addition in the direction contrary to Michael's rule.

(iii) (Compare rule *c*, p. 1869.) The effect of the introduction of an  $\alpha$ -substituent into the acrylic ester residue may be deduced on similar lines, and corresponds with rule *c* (for examples, see especially papers 1, 3, and 6).

Other reversible additive reactions, such as the aldol reaction, can be subjected to a similar analysis. In advancing these explanations and those in the papers cited, the authors gratefully acknowledge the influence of the writings of Thiele, Werner, Flürscheim, Michael, Lapworth, Decker, Robinson, Vörländer, Lewis, Eastman, and others to whom detailed reference has not been practicable.

THE UNIVERSITY, LEEDS.

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